Embryology of the Face and Skull

Carlson, Bruce M. Human Embryology and Developmental Biology 3rd Edition 2004

Pharyngeal Arches, Face, and Skull

Early Events in the Development of the Head & Neck

- Development of the head and neck begins during gastrulation as epiblast cells that pass through the primitive node and primitive pit begin to organize themselves as the **notochord** and **prechordal plate** caudal to the **oropharyngeal membrane**.
- As the notochord forms in a cranial to caudal direction, the overlying neural plate begins folding into the **neural tube** and the mesoderm immediately adjacent to it on either side becomes organized into thickened columns of **paraxial mesoderm**.
- As the cranial neural tube fuses, it becomes divided into its forebrain, midbrain and hindbrain components. The **isthmus signaling center** forms at the level of the midbrain/hindbrain boundary and the hindbrain becomes segmented into **eight rhombomeres**.
- As these tissues become increasingly more organized, signals from the notochord & hindbrain induce formation of the **otic placode** from surface ectoderm lateral to the presumptive hindbrain (specifically adjacent to rhombomeres 5 and 6).
- Caudal to the otic placode, the paraxial mesoderm becomes further organized into **somites** and the more lateral mesoderm becomes organized into **intermediate mesoderm** and **lateral plate mesoderm**.
- Cranial to the otic placode, the paraxial mesoderm remains as an unsegmented single column, and the **intermediate and lateral plate mesoderm do not form**.
- With differential growth of the brain vesicles, the forebrain overgrows the oropharyngeal membrane and the anterior head region folds ventrally, bringing the oropharyngeal membrane ventrally (along with the precardiac mesenchyme and septum transversum), and pinching off the **foregut** (primitive pharynx) from the yolk sac.

Formation of the Pharyngeal Arches

- During neurulation, cells at the crests of the neural folds (**neural crest cells**) undergo an epithelial-to-mesenchymal transformation, lose cell-to-cell adhesiveness, and migrate away from the neural tube. As in the trunk, some of the neural crest cells that leave the cranial neural folds will migrate along stereotypical dorsolateral, ventrolateral and ventral pathways and differentiate as neurons of the sensory and autonomic ganglia, or as the melanocytes of the face and scalp. Neural crest cells from the cranial neural tube will also give rise to the **type I cells of the carotid body** and, perhaps, the **parafollicular cells** of the thyroid gland.
- In the cranial region, cranial neural crest (CNC) cells leave the neural folds in large streams to surround the primitive pharynx; these large collections of cells then proliferate to form the **pharyngeal** (branchial or visceral) **arches**.
- A total of six such swellings form (numbered 1-6 in a cranio-caudal direction), but the fifth arch degenerates soon after it forms, leaving only five identifiable arches (numbered 1-4 and 6).
- CNC follows specific pathways of migration:
  - CNC from rhombomeres 1 and 2 and the caudal midbrain populate the first arch (the mandibular arch)
  - CNC from rhombomere 4 populates the second arch (the hyoid arch)
  - CNC from rhombomeres 6 and 7 populate the remaining arches (3, 4 and 6)
  - Neural crest cells that migrate from cranial midbrain and caudal forebrain populate the

frontonasal prominence which borders the oropharyngeal membrane cranially; caudally, the oropharyngeal membrane is bounded by the mandibular arch. As these swellings continue to expand they define the **stomodeum** (primitive mouth) of the embryo.

The Anatomy of a Pharyngeal Arch

- The pharyngeal arches are separated from one another externally by **pharyngeal grooves** (clefts) and internally by **pharyngeal pouches**.
- The lining of the pharyngeal grooves is **surface ectoderm** while that of the internal pharyngeal pouches is **foregut endoderm**. Each ectodermal pharyngeal groove corresponds with each endodermal pharyngeal pouch, with a layer of mesenchyme intervening.
- The core of each arch is composed of mesenchyme derived from two sources: 1) the CNC derived mesenchyme or **ectomesenchyme**; and 2) **paraxial mesoderm**. The ectomesenchyme will give rise to all of the connective tissues of the face except the enamel of the teeth (e.g., bone, dentin, cartilage, connective tissue sleeves of cranial musculature). Connective tissues of the neck are formed from both ectomesenchyme and lateral plate mesoderm. The paraxial mesoderm will give rise to most of the head and neck musculature.
- In addition to mesenchyme, each pharyngeal arch also contains a basic set of structures:
  - ➢ A central **cartilage** rod that forms the skeleton of each arch.
  - ➢ A vascular component, an **aortic arch artery** that runs around the pharynx from the ventrally located heart to the dorsal aorta.
  - ➢ A **nervous element**, consisting of sensory and special visceral motor fibers of one or more cranial nerves, that **supplies all of the derivatives of that arch**.

Fate of the Pharyngeal Grooves

- Only the first pair of pharyngeal grooves contributes to adult structures. The dorsal end of this groove deepens to form the **external acoustic meatus**. The ecto-meso-endodermal membrane in the depth of the groove persists as the **tympanic membrane**.
- The remaining grooves become obliterated by a caudal overgrowth of the second arch that provides a smooth contour to the neck and forms the **cervical sinus** behind. This sinus becomes obliterated as neck development continues. If not, a **cervical cyst** or **cervical fistula** may result.

Fate of the Pharyngeal Pouches

- **First pharyngeal pouch**: This pouch expands into an elongate **tubotympanic recess** that will form the tympanic cavity (separated from the first pharyngeal groove by the tympanic membrane) and the mastoid antrum. Its connection with the pharynx gradually elongates to form the **auditory tube**.
- **Second pharyngeal pouch**: The dorsal portion of this pouch persists in an attenuated form as the tonsillar fossa, the endodermal lining of which differentiates as the **palatine tonsil**.
- **Third pharyngeal pouch**: This pouch expands into a solid dorsal bulbar portion and a hollow ventral elongate portion. Each dorsal portion differentiates into an **inferior parathyroid gland**. The ventral portion fuses with the opposite side to form the **thymus**. The thymus and parathyroid glands migrate caudally. The parathyroid glands separate from the thymus gland and reach the dorsal surface of the thyroid gland which has descended from the developing tongue (see below).
- **Fourth pharyngeal pouch**: This pouch also expands into a dorsal bulbar portion and a ventral elongate portion. Each dorsal portion develops into a **superior parathyroid gland**. The fate of the ventral portion is uncertain.
- **Fifth pharyngeal pouch**: This pouch appears as a diverticulum of the fourth pouch and develops into an **ultimobranchial body** (or postbranchial body), which is the source of the parafollicular cells of the thyroid, gland. Later these cells become incorporated into the thyroid gland.

Development of the Thyroid

- The thyroid initially appears as a median endodermal thickening in the floor of the primitive pharynx between the first and second pouches. Shortly thereafter, this **thyroid primordium** descends through the tissues of the neck.
- Early in its descent the thyroid primordium remains connected to the pharynx by the **thyroglossal duct**. This duct eventually breaks down and the developing thyroid continues to descend in the neck until it reaches its final destination just inferior to the cricoid cartilage of the larynx.
- Remnants of the thyroglossal duct may persist in the form of a **thyroglossal duct cyst**. Usually the only remnant of thyroid duct is its original opening - the **foramen cecum** of the tongue.
- As the thyroid descends within the neck it picks up the superior and inferior parathyroid glands, as well as the parafollicular cells of the ultimobranchial body.

Fate of the Pharyngeal Arches

- **Pharyngeal Arch 1**: The mandibular arch is the largest of the pharyngeal arches and is involved, along with the frontonasal prominence, in the development of the face (see below). The maxilla is derived from a small maxillary prominence extending cranioventrally from the much larger mandibular prominence. The cartilage of the first arch, **Meckel's cartilage**, provides a template for subsequent development of the mandible, but most of its cartilage substance disappears in the formed mandible. Persisting portions of Meckel's cartilage include major portions of the **malleus** and **incus**, as well as the **sphenomandibular ligament**. The musculature of the mandibular arch subdivides and migrates to form the **muscles of mastication** (i.e., mylohyoid, anterior belly of digastric, tensor tympani and tensor veli palatini) **all of which are innervated by the mandibular division of the trigeminal nerve (CN V).**
- **Pharyngeal Arch 2**: The cartilage of the hyoid arch (Reichert's cartilage) forms most of the **stapes** and contributes to the **styloid process** of the temporal bone, the **stylohyoid ligament**, and the **lesser horn and cranial part of the body of the hyoid bone**. Muscles derived from this arch include the **stapedius**, the **stylohyoid**, the **posterior belly of digastric** and the **muscles of facial expression**, **all of which are innervated by the facial nerve (CN VII)**.
- **Pharyngeal Arch 3**: The cartilage of this small arch produces the **greater horn and caudal body of the hyoid bone**. The mesenchyme forms the **stylopharyngeus muscle, the only muscle innervated by the glossopharyngeal nerve (CN IX).**
- **Pharyngeal Arches 4 and 6:** The cartilages of these arches form the **laryngeal cartilages** (i.e., thyroid and cricoid) and may contribute to the superior tracheal rings. Muscles derived from these arches are those muscles of the palate, pharynx and larynx that receive their motor innervation from the **vagus nerve (CN X)**.

Development of the Face and Palate

- Initially the primitive mouth, or **stomodeum**, is separated from the cranial foregut by the **oropharyngeal membrane**. At about 24 days of development this membrane ruptures to establish communication between the digestive tract and the amniotic cavity.
- The face develops from five facial primordia which form around the stomodeum.
  - A single **frontonasal prominence** forms the cranial boundary of the stomodeum.
  - Paired **maxillary prominences** of the first pharyngeal arch form its lateral boundaries.
  - Paired **mandibular prominences** of the first arch form its caudal boundary.
- The lower jaw and lip are very simply formed by midline merging of the paired mandibular prominences and are the first parts of the face to become definitively established.
- Establishment of the upper jaw is more complex.
  - The frontonasal prominence surrounds the forebrain which has already sprouted lateral

optic diverticula that will form the eyes.

- At the inferolateral corners of the frontonasal prominence, thickened **nasal placodes** arise. These ectodermal placodes appear to invaginate as inverted horseshoe-shaped masses of cells, the **medial** and **lateral nasal ridges**, proliferate around them.
- Fusion of the medial nasal ridges with the maxillary prominences provides for continuity of the upper jaw and lip and separation of the nasal pits from the stomodeum.
- The fused medial nasal ridges and frontonasal prominence form the **philtrum** of the upper lip, tip of the nose, and the **primary palate** of the upper jaw (where upper incisor teeth will form).
- The lateral nasal ridge and maxillary prominence are initially separated by a deep furrow. As the lateral nasal ridge and maxillary prominence fuse, the epithelium in the floor of the groove between them forms a solid core that separates from the surface and comes to lie deep to the remnants of the groove. Eventually this rod canalizes to form the **nasolacrimal duct**.
- The palate develops from both the **primary palate**, formed by the midline merging of the medial nasal prominences, and the **secondary palate**, which develops from two internal projections of the maxillary prominences, the **vertical palatine shelves** (a.k.a., processes). Initially the latter structures project inferomedially on each side of the developing tongue. As the jaws continue to develop and grow, the tongue moves inferiorly and the lateral palatine processes elevate into a horizontal position. Once elevated, the **horizontal palatine shelves** grow towards one another and fuse. They also fuse with the primary palate anteriorly and the nasal septum superiorly.
- Among the numerous genes regulating development of the upper jaw is **Sonic hedgehog** (**Shh**). Loss of Shh signaling at this stage of facial development inhibits their growth and leads to **hypotelorism** (mediolateral narrowing of the frontonasal process) and cleft lip/palate. Overexpression of Shh in the facial primordia results in **hypertelorism** (a mediolateral widening of the frontonasal process and a widening between the eyes). In extreme cases, excess Shh can lead to a duplication of midfacial structures.

Development of the Tongue

- Tongue development begins when a median elevation, the median tongue bud or **tuberculum impar**, becomes visible in the floor of the first pharyngeal arch, just rostral to the **foramen cecum**.
- On either side of this structure develop two oval **distal tongue buds** that rapidly increase in size, merge with one another and overgrow the median bud. The fused distal tongue buds form the **anterior two-thirds** or **oral part** of the tongue. The plane of fusion of the distal buds in the adult is the **median sulcus** of the tongue. As a derivative of the first pharyngeal arch, the mucosa of the oral part of the tongue receives its general somatic afferent innervation from the **trigeminal nerve** (CN V). Special visceral afferent (taste) innervation of the oral tongue is provided by the **facial n.** (CN VII)
- The posterior third of the tongue (pharyngeal part) and the root of the tongue are initially indicated by the **copula (or hypobranchial eminence), an elevation of the floors of the third arch and most cranial aspect of the fourth arch**. With further development the hypobranchial eminence overgrows the second arch entirely and fuses with the mucosa of the oral tongue. The line of fusion of the anterior and posterior parts of the tongue is roughly indicated by the v-shaped groove called the **terminal sulcus**. The mucosa of the pharyngeal tongue receives its GSA and SVA innervation from the **glossopharyngeal nerve** (CN IX). The root of the tongue receives its GSA and SVA innervation from the **vagus nerve** (CN X).
- Most of the musculature of the tongue is derived from myoblasts that migrate from the **myotomes** of the **occipital somites**. These myoblasts migrate into the tongue, where they differentiate into muscle fibers. The **hypoglossal nerve** accompanies the myoblasts during their

migration and innervates the tongue muscles once they have formed.

Development of the Skull

- The bones of the skull not derived from pharyngeal arch cartilages (i.e., all but the middle ear ossicles, styloid process, mandible, portion of maxilla, and hyoid) arise through both **endochondral** and **intramembranous ossification**.
- Of endochondral origin are the portions of the bones that form the basicranium. These elements are derived from a series of cartilages that form inferior to the developing brain, around the anterior tip of the notochord. With the exception of occipital portion of the basicranium, which is derived from the **sclerotomes** of the cranial-most four somites (**occipital somites 1-4**), the cells that form the **chondrocranium** are of neural crest origin.
- All remaining bones of the skull are of intramembranous origin and all but the parietals, squamous portions of the occipital and temporal bones, and mastoid and tympanic portions of the temporals are of neural crest origin.
- Ossification of skull bones begins at definable locations termed **centers of ossification**. During development, the growing ossification centers coalesce to form recognizable bones. In the mandible, at its **cranial articulation** (the condyle), a cartilage develops instead of bone. This **secondary cartilage**, which forms intramembranously and is therefore distinct from the **primary cartilage** of the basicranium, will serve as a site of mandibular growth until it too ossifies (endochondrally).
- Due to the large size of the human brain, complete ossification of the calvarial bones is delayed until after birth. As a consequence, the calvarial bones of the newborn infant are separated from one another by large areas of unossified membrane called **fontanelles**. The presence of these fontanelles allows the bones to override one another as the baby passes through the birth canal. The shape of the calvarium returns to normal shortly after birth.
    - The **anterior fontanelle** is located at the junction of the sagittal, coronal and frontal sutures.
    - The **posterior fontanelle** is triangular and is bounded by the parietal bones anteriorly and the occipital bones posteriorly.
    - In addition, newborn crania also display two **sphenoidal** (anterolateral) and two **mastoid** (posterolateral) fontanelles.
- In the skull, individual bones are separated from one another by **sutures**. Found exclusively in the cranium, sutures are fibrous joints that allow very limited movement. Instead, the function of sutures is to allow for expansion of the growing brain, oculus and extraocular tissues, nasal epithelium and oral cavity. In addition, sutures maintain populations of osteoblasts and are therefore additional sites of bone and cranial growth. As the soft tissues of the skull mature, sutural growth ceases and the sutures eventually fuse. In some genetic disorders sutures of the calvarium fuse prematurely. Such **craniosynostosis** usually results in cranial deformities since the skull must adjust to this loss of growth potential by exaggerating growth at alternative locations (i.e., at other sutures).